based on the value of a crossover index or the ratio between a marker associated with the phase of osteoblast proliferation and matrix formation and the measured value of the marker that reflects the action of osteoclasts, or on the value of a crossover index or the ratio between a marker associated with the phase of calcification and a marker associated with the phase of matrix maturation and the measured value of a marker associated with bone type I collagen,

whereby the amelioration of bone metastasis or therapeutic effect and the degree of the exacerbation of bone metastasis are diagnosed correctly by monitoring said two markers, one associated with osteoblasts and targeted to evaluation of therapeutic effect, and the other associated with osteoclasts and targeted to evaluation of worsening of the disease.

Amend the claims as follows:

2. (amended) The method of claim 6, wherein the marker that reflects the activity of osteoblasts is:

(1) a marker associated with the phase of osteoblast proliferation and matrix formation and a marker associated with the phase of calcification; or

(2) a marker associated with the phase of matrix maturation and a marker associated with the phase of calcification.

3. (twice Amended) The method according to claim 6, wherein the marker that reflects the activity of osteoblasts is:

C3

(1) Carboxyterminal propeptide of type I procollagen or Amino terminal propeptide of type I procollagen and osteocalcin; or

(2) Bone specific alkaliphosphatase and osteocalcin.

4. (amended) The method according to claim 6,

C4

wherein the marker that reflects the action of osteoclasts is a marker associated with bone type I collagen.

5. (Amended) The method according to claim 6,

C5

wherein the marker that reflects the action of osteoclasts is deoxypyridinoline and/or Carboxyterminal telopeptide of type I collagen.

In place of now cancelled claim 1, add new claim 18 as follows:

C6

18. (new) The method according to claim 3, wherein the marker that reflects the action of osteoclasts is a marker associated with bone type I collagen.

REMARKS

The final Official Action of January 29, 2002, has been carefully studied. Upon entry of the present amendment,